PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Rajesh Suresh KSHIRSAGAR et al. Group Art Unit: 1616

Application No.: 10/642,194 Examiner: S. QAZI

Filed: August 18, 2003 Docket No.: 116875

For: SUSTAINED RELEASE PHARMACEUTICAL COMPOSITION OF A CEPHALOSPORIN ANTIBIOTIC

REQUEST FOR RECONSIDERATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In reply to the March 27, 2006 Office Action, reconsideration of the rejection is respectfully requested in light of the following remarks.

Claims 1-6, 8-16, 19 and 20 are pending in this application. Claims 19 and 20 are withdrawn from consideration. Applicants respectfully point out that claim 7 was cancelled in the Amendment filed on December 13, 2005.

I. Double Patenting Rejection

Claims 1-16 were rejected under the judicially created doctrine of double patenting over claims 1-3, 5 and 6 of U.S. Patent No. 6,932,981 ("Sen"). This rejection is respectfully traversed.*

Applicants submit that claims 1-6 and 8-16 are patentable over claims 1-3, 5 and 6 of Sen, and in fact are patentable over the entire disclosure of Sen. Applicants submit that none

* The present application is not assigned to the same assignee as Sen.

of the polymers recited in the claims of, or described in, Sen for the outer and inner coatings are neutral swellable polymers because these polymers of Sen contain either a carboxyl functional group (outer coating) or a quaternary ammonium functional group (inner coating). In contrast, the neutral swellable polymers recited in claim 1 have no functional group (i.e., the swellable polymer is neutral).

Also, none of the outer or inner polymer coatings claimed in Sen is a galactomannan. Contrary to the Patent Office's allegation, nothing in Sen provides any motivation to provide galactomannans in either coating. This rejection is based on unsupported allegations.

Moreover, Sen describes and claims a fast disintegrating controlled release composition comprising a core material containing cefuroxime axetil present as controlled release form; provided with an outer coating of a copolymer selected from aqueous dispersions of enteric methacrylic acid and methacrylic acid esters anionic copolymers having a carboxyl group as the functional group (such as Eudragit® L and S) and an inner coating of sustained release copolymer selected from aqueous dispersions of acrylate and methacrylate pH independent copolymers having a quaternary ammonium group as the functional group.

The combination of polymers described and claimed in Sen is a combination of pH dependent and pH independent polymers. The outer coating comprises aqueous dispersions of methacrylic acid copolymers with carboxyl groups (such as Eudragit® L and S), which are soluble above pH 5.5 and 7.0 respectively (these are pH dependent polymers). The inner coating comprises aqueous dispersions methacrylic acid copolymers having a quaternary ammonium functional group (these are pH independent).

In contrast, the pH independent polymers recited in claim 1 belong to a different chemical class and behave differently in gastric fluids. Xanthan gum (galactomannans) is a naturally occurring anionic heteropolysaccharide gum derived from aerobic fermentation of *Xanthomanas campestris*. It contains D-glucose, D-mannose, D-glucuronate in the molar ratio

of 2.8:2.0:20 and is partially acetylated with about 4.7 acetyl. It is a viscolyzing agent and helps to maintain the integrity of the dosage form along with helping the sustained release of the drug from the matrix. The viscosity of an aqueous solution of xanthan gum is not significantly affected by changes in the pH of the solution between 1 and 11 (i.e., it is pH independent).

Another polymer used in the combination in the present application is Eudragit® NE 30 D poly (ethyl acrylate : methyl methacrylate) 2:1 (see claim 8), which is basically a methacrylic ester copolymer and has no functional group as compared to the copolymers described and claimed in Sen. The two type of polymers used in the present application chemically belong to different classes unlike the polymers described and claimed in Sen, where both polymers belong to the same group of methacrylic acid copolymers.

The two polymers used in the present application also differ in their physical characteristics. Specifically, xanthan gum is soluble in water, while Eudragit NE® 30 D remains water insoluble throughout the entire pH range of the gastrointestinal tract. Applicants thus submit that one of ordinary skill in the art would not have combined the pH independent polymers, the xanthan gum and the Eudragit® NE 30 D, which belong to different chemical classes and have different physical characteristics. In other words, one of ordinary skill in the art would not have been able to predict how the pH independent polymers would behave in varying chemical environments along the gastrointestinal tract and their release mechanism. Applicants submit that Sen does not claim, teach or suggest the combination of polymers recited in claims 1-6 and 8-16.

For the foregoing reasons, Applicants submit that claims 1-6 and 8-16 are patentable over Sen. Reconsideration and withdrawal of the rejection are thus respectfully requested.

II. Rejection Under 35 U.S.C. §103(a)

Claims 1-16 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,948,440 ("Arora") and U.S. Patent No. 6,083,532 ("Zhang"). This rejection is respectfully traversed.

The Patent Office alleges that Arora teaches a pharmaceutical composition for controlled release of an active ingredient, said composition comprising cefaclor, cephalexin, or their pharmaceutically acceptable hydrates, salts or ester as the active ingredient, and a mixture of hydrophilic polymers of different viscosity grades. The Patent Office appears to be relying on Zhang to teach the polymer mixture as recited in the present claims. Zhang teaches drug formulations comprising a pharmaceutical and a three component release rate controlling matrix composition. The three components of the matrix composition are: (1) a pH dependent gelling polymer such as an alginate component, (2) an enteric polymer component, such as Eudragit® L or S, and (3) a pH independent gelling polymer, such as hydroxyl propyl methyl cellulose or polyethylene oxide. See the Abstract. As a further example of a pH independent gelling polymer, Zhang teaches xanthan gum. Col. 2, lines 6-10. Applicants respectfully submit that Arora and Zhang, in combination or alone, do not teach or suggest all of the features recited in claims 1-16.

The polymers taught by Arora are a combination of cellulose derivatives like hydroxy propyl methyl cellulose and hydroxy propyl cellulose. The present claims are directed towards a combination of galactomannans and neutral swellable polymers. Applicants submit that none of the polymers taught by Arora is a galactomannan or a neutral swellable polymer as recited in claim 1.

The neutral swellable polymer, i.e., the acrylic copolymer of the present application, is distinctly different from the cellulose polymers taught by Arora because they belong to different classes and possess different properties. The polymers taught by Arora are cellulose

polymers and are water soluble (hydrophilic). In contrast, the neutral swellable polymers of the present application include acrylic copolymers, which are insoluble over the entire pH range (hydrophobic). Arora thus does not describe the use of neutral swellable polymers.

Applicants submit that Zhang does not remedy the deficiencies of Arora. Zhang teaches a matrix composition having: (1) a pH dependent gelling polymer such as an alginate component, (2) an enteric polymer component, such as Eudragit® L or S, and (3) a pH independent gelling polymer, such as hydroxy propyl methyl cellulose or polyethylene oxide. The drug release rate can be adjusted by changing the amount of one or more of these components of the composition.

Zhang also does not teach the use of any neutral swellable polymers.

First, Applicants submit that the Eudragit® L or S taught by Zhang are not neutral swellable polymers, as they contain carboxyl functional groups. Such polymers are soluble above a pH of 5.5 and 7.0, respectively. In other words, the polymers taught by Zhang are pH dependent polymers, and are not neutral swellable polymers as required in claim 1. The neutral swellable polymers recited in claim 1 have no functional group (i.e., they are neutral) and are thus insoluble over the entire pH range and pH independent.

In addition, Applicants submit that the polymer recited in claim 8 (e.g., Eudragit® NE 30 D) is not an enteric polymer as in Zhang because the recited polymer is insoluble over the entire pH range, whereas enteric polymers are soluble at a pH above 5.5. The different Eudragit® materials described in Zhang are not neutral swellable polymers as discussed above.

Second, pH dependent gelling polymers such as alginates are not and do not comprise neutral swellable polymers as recited in the present claims. As explained above, neutral swellable polymers have no functional groups and are thus insoluble over the entire pH range.

Thus, neutral swellable polymers as recited in the present claims are pH independent. This is clearly different from the pH dependent alginates taught by Zhang.

Third, the pH independent gelling polymer, such as a hydroxy propyl methyl cellulose or polyethylene oxide, is also not a neutral swellable polymer. As described above, such polymers are water soluble (hydrophilic). In contrast, the neutral swellable polymers of the present application include acrylic copolymers, which are insoluble over the entire pH range (hydrophobic).

Furthermore, Zhang does not teach a controlled release composition of a cephalosporin antibiotic as required in claim 1.

Thus, even if Arora and Zhang were to have been combined as alleged by the Patent Office, the sustained release composition recited in the present claims would not have been achieved. Specifically, Arora and Zhang, in combination or alone, do not teach or suggest a composition including neutral swellable polymers at all, much less in combination with galactomannans.

For at least the foregoing reasons, Applicants submit that Arora and Zhang, in combination or alone, do not teach or suggest all of the features recited in claims 1-6 and 8-16. Reconsideration and withdrawal of the rejection are thus respectfully requested.

III. Rejoinder

Withdrawn process claims 19-20 depend from product claim 1 and include all of its limitations. MPEP §821.04 states that if Applicants elect claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. Because process claims 19 and 20 include all of the limitations of product claim 1, claims 19 and 20 must be rejoined and examined with claim 1 upon allowance of claim 1. Furthermore, Applicants understand that upon search, examination, and allowance of the elected species,

search and examination will continue as to the non-elected species within the scope of the generic claims.

IV. Conclusion

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1-6, 8-16, 19 and 20 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

Leana Levin

James A. Oliff
Registration No. 27,075

Leana Levin
Registration No. 51,939

JAO:LL/can

Date: June 27, 2006

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461